

Remarks:

Claims 1-3, 6-10 and 21-22 are pending. Claims 3 and 6 have been editorially amended.

Applicants and the undersigned thank the Examiner for the telephone interview of April 30, 2007, in which the outstanding office action was discussed.

No issues of new matter should arise and entry of the amendment is respectfully requested.

I. Priority

Applicants agree with the Examiner that the elected subject matter of nitrosated ACE inhibitors currently undergoing prosecution in the present application is entitled to the benefit of the January 31, 2000 filing date of U.S. Provisional Application 60/179,020.

II. Objection to Claims

Claim 1 is objected to for reciting the phrase “therapeutically effective amount” instead of a particular dose or range of dose. Applicants respectfully traverse this objection and submit that one skilled in the art would be able to determine the appropriate dose using standard clinical techniques as described in, for example, The Physician’s Desk Reference by Goodman and Gilman, which is referred to in the specification on page 36, in the paragraph starting on line 25. As further described in the specification on pages 36-37, one skilled in the art would be able to determine and adjust the dose accordingly depending on patient profile, pharmacological considerations, route of administration, and other factors.

Applicants respectfully submit that, given the guidance provided in the specification and the knowledge available to the skilled artisan, one skilled in the art would readily be able to determine what a therapeutically effective amount of a particular nitrosated ACE inhibitor would be for the treatment of a particular vascular disease characterized by nitric oxide insufficiency in a patient in need thereof. In view thereof, respectfully request that the objection to the claims be withdrawn.

III. Rejection under 35 U.S.C. §112, First Paragraph

Claims 1-10 and 21-22 are rejected under 35 USC § 112, first paragraph, as lacking enablement and failing to comply with the written description requirement.

Applicants respectfully traverse the rejection and respectfully submit that the claims satisfy the requirements under 35 U.S.C. § 112, first paragraph.

The Examiner asserts that the specification provides adequate description of, and is enabled for, treatment of a vascular/cardiovascular disease via administering an angiotensin converting enzyme (ACE) inhibitor or a nitrosated compound that is not an ACE inhibitor, but does not provide adequate description of, and is not enabled for, treatment with a nitrosated ACE inhibitor or solid dosage forms thereof.

Applicants respectfully submit that one of skill in the art would understand how to prepare nitrosated ACE inhibitors from any and all of the parent ACE inhibitors listed in the specification on page 30. The specification at page 29, lines 19-26, discloses that a nitrosated compound refers to any compound that has been nitrosated through one or more sites such as oxygen (hydroxyl condensation), sulfur (sulfhydryl condensation), and/or nitrogen. As discussed during the telephone interview with the Examiner, Applicants have described in the specification at page 29, lines 27-30 to page 30, lines 1-2, how the skilled artisan could readily use conventional techniques known in the arts and in available publications to prepare the nitrosated compounds. For example, known methods for nitrosating compounds are described in U.S. Patent Nos. 5,380,758, and 5,703,073; WO 97/27749; WO 98/19672; Oae et al., *Org. Prep. Proc. Int.*, 15(3):165-198 (1983); and WO 98/21193. As the Examiner pointed out during the interview, WO 99/00361 is also referred to in the specification on page 30; however, Applicants respectfully submit that this reference is provided for its disclosure of nitrate salts of ACE inhibitors, which are not the same as nitrosated ACE inhibitors, as discussed further below with respect to the 102/103 rejection.

Applicants have also demonstrated a method of treating a cardiovascular disease through administration of a nitrosated ACE inhibitor or a salt thereof, as provided in the specification at page 4, lines 1-7, and page 22, lines 25-30 to page 23, line 1. Moreover, Applicants respectfully submit that the specification provides adequate guidance on making solid dosage forms of the nitrosated ACE inhibitors and methods of administering the dosage forms to a patient in need thereof. As discussed above, Applicants submit that one skilled in the art would be able to determine the appropriate dose using standard clinical techniques as described in, for example,

The Physician's Desk Reference by Goodman and Gilman, which is referred to in the specification on page 36, in the paragraph starting on line 25. As further described in the specification on pages 36-37, one skilled in the art would be able to determine and adjust the dose accordingly depending on patient profile, pharmacological considerations, route of administration, and other factors.

In view thereof, Applicants respectfully submit that the claims satisfy the requirement under 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection under this provision be withdrawn.

IV. Rejection under 35 U.S.C. §112, Second Paragraph

Claims 1-10 and 21-22 are rejected under 35 USC § 112, second paragraph, as being indefinite. Applicants respectfully traverse the rejection and submit that the claims are not indefinite.

The Examiner states that the recitation “characterized by” in claim 1 is unclear. In view thereof the term “characterized by” has been replaced by “resulting from”.

Applicants respectfully submit that claim 21 does further limit the subject matter claimed in claims 1, 3, and 7. Claim 21 recites a method of claim 1, further comprising administering to the patient a therapeutically effective amount of at least one compound used to treat a cardiovascular disease or a pharmaceutically acceptable salt thereof. The specification defines a “compound used to treat a cardiovascular disease” at page 14, lines 13-28 to page 15, lines 1-11. Applicants submit that claims 1, 3, and 7 do not include the limitation of the further administration of a compound used to treat a cardiovascular disease. In view thereof, claim 21 does further limit claims 1, 3, and 7 and correction is not required.

Applicants respectfully submit that claim 22 does not lack sufficient antecedent basis. The recitation of “wherein the compound used to treat the cardiovascular disease is a beta-adrenergic blocker, a cholesterol reducer, ...or a mixture of two or more thereof” in claim 22 refers back to and further limits the “compound used to treat a vascular disease” limitation of claim 21. Applicants submit that claims 1 and 21 do not refer to “a beta-adrenergic blocker, a cholesterol reducer, ...or a mixture of two or more thereof” because this limitation is not the subject matter that is being further limited by claim 22 and therefore correction is not required.

In view of the above, Applicants respectfully submit that the claims satisfy the requirement under 35 U.S.C. § 112, second paragraph, and respectfully request that the rejection under this provision be withdrawn.

V. Rejection under 35 U.S.C. §102/103

Claims 1-10 and 21-22 are rejected under 35 U.S.C. §102 as being anticipated by, or in the alternative, under §103 as obvious over Del Soldato (WO 99/00361, also US 218,417 B1).

Applicants respectfully traverse the rejection and submit that the claimed invention is not anticipated by and is unobvious over Del Soldato.

The present claims are directed to methods of treating a vascular disease characterized by nitric oxide insufficiency by administration of a therapeutically effective amount of at least one nitrosated ACE inhibitor.

Del Soldato teaches nitrate salts of ACE inhibitors. Del Soldato does not teach nitrosated ACE inhibitors, wherein the NO₂ group is covalently linked to the parent ACE inhibitor through one or more sites such as oxygen (hydroxyl condensation), sulfur (sulfhydryl condensation), and/or nitrogen. One of skill in the art would understand that a nitrate salt comprises an ionic linkage between the charged nitrate group and the ionized parent compound. Therefore, Applicants submit that Del Soldato's ACE inhibitor nitrate salts do not anticipate the claimed nitrosated ACE inhibitors.

Moreover, Applicants respectfully submit that the claimed nitrosated ACE inhibitors are not obvious in view of Del Soldato's ACE inhibitor nitrate salts. One of skill in the art would understand that covalent bonds are completely different from ionic bonds. Applicants submit that one would not be motivated, much less expect to be able to successfully prepare, nitrosated ACE inhibitors in view of the disclosure of Del Soldato.

In view of the above, Applicants respectfully submit that the presently claimed invention is neither anticipated by nor obvious over Del Soldato, and respectfully request that the rejection under 35 U.S.C. § 102/103 be withdrawn.

VI. Rejection under 35 U.S.C. §103

Claims 1-10 and 21-22 are rejected under 35 U.S.C. §103 as being obvious over Del Soldato (WO 99/00361, also US 218,417 B1) in view of Chobanian (US 5,645,839).

Applicants respectfully traverse the rejection and submit that the claimed invention is not unobvious over Del Soldato in view of Chobanian.

As discussed above, the present invention is directed to methods using nitrosated ACE inhibitors. Del Soldato does not teach or suggest nitrosated ACE inhibitors. Chobanian, relied upon in the Office Action for teaching sustained release dosages, does not cure the deficiencies of Del Soldato. Applicants respectfully submit that the cited references, individually or in combination, do not disclose or suggest, or provide motivation to arrive at the presently claimed invention.

In view of the above, Applicants respectfully submit that the presently claimed invention is not obvious over Del Soldato in view of Chobanian, and respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

VII. Conclusion

Applicants respectfully request reconsideration and allowance of claims 1-3, 6-10 and 21-22.

Examiner Srivastava is encouraged to contact the undersigned concerning any questions about the present application.

Respectfully submitted,



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